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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,712	03/30/2001	Gregor Sagner	5443	7485

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 01/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,712	SAGNER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17,23-26 and 31-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on November 29, 2004, has been entered.

2. Claims 1-14, 18-22, 27-30 are cancelled. New claims 40-41 are added. Claims 15-17, 23-26, 31-41are pending

3. This application is filed on March 30, 2001 which claims priority to foreign priority to European patent application 00 107 036.6 filed on 3/31/2000, Germany patent application 100 34 209.4 filed on 7/13/2000 and 100 45 512.2 filed on 9/13/2000.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 15-16, 23-26, 31-35, 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al. (WO 99/54510) in view of Zhang et al. (USPN. 6,235,504).

Lowe et al. teach a method for determining a quantitative measure of an amplification of a target nucleic acid of claims 15-16, 23-26, 31-33, 38-39 comprising the steps of

(a) preparing a dilution series of the target nucleic acid (see page 3, line 12-14, page 6, line 20-28, page 11, line 24-35);

(b) amplifying the target nucleic acid under defined conditions and measuring the amplification in real-time (see page 3, line 14-25);

(c, d) setting a defined signal threshold value and determining for each dilution, the cycle number at which the signal threshold value is exceeded (threshold cycle for each dilution) (see page 3, line 25-27, page 10, line 16-23);

(f) calculating the amplification equivalent in each dilution series and normalizing the RNA equivalent to provide normalized RNA equivalent standard curve. (see page 3, line 29-33, page 10, lines 31-39).

With regard to claim 23, 25, Lowe et al. teach determining concentration of the target nucleic acid (see page 12, line 9-15);

With regard to claim 31-33, Lowe et al. teach quantifying the amount of target nucleic acid relative to the reference nucleic acid (see page 13, line 30-39, page 14, line 1-19);

With regard to claims 38- 39, Lowe et al teach a method for quantitation of a target nucleic acid using internal standard or reference nucleic acid (see page 13, line 10-39);

With regard to claims 34-35, 40-41, Lowe et al. teach said amplified nucleic acid is detected using fluorescently labeled probe such as TAQMAN probes or FRET probes (see page 10, line 1-30, page 8, line 29-36).

However, Lowe et al. did not teach determining a non-linear continuously differentiable function of a logarithm of copy number.

Zhang et al. teach a method for determining amplification efficiencies for different DNA samples by real-time PCR, wherein Zhang et al. teach that the method comprises correlating the threshold cycle (derived from real-time PCR using molecular beacons) and the initial concentration of DNA templates up to six log dilutions from 10^8 to 10^2 molecules per PCR and measuring the ratio of reference nucleic acid and a target nucleic acid by plotting threshold cycles measured for the reference and the target nucleic acid (see col. 9, line 7-36).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of determining quantitative measure of an amplification of a target nucleic acid as taught by Lowe et al. with the step of calculating the logarithm of copy number in relation to a reference nucleic acid as taught by Zhang et al. to achieve expected advantage of developing an improved sensitive method for determining the efficiency of an amplification of a target nucleic acid. An ordinary person skilled in the art would have had a reasonable expectation of success that the combination would result in achieving said expected advantage because Zhang et al. explicitly taught that the correlation between the threshold cycle and the initial concentration of DNA templates provides precise measurement of abundance of target nucleic acids (see col. 9, line 7-25). An ordinary practitioner would have been motivated to combine the method of determining a quantitative measure of a target nucleic

acid as taught by Lowe et al. with the inclusion of the step of determining the definable function of logarithm of copy number for the purpose of enhancing the sensitivity and efficiency in the quantitation of said target nucleic acid in a sample.

B. Claims 17, 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al. (WO 99/54510) in view of Zhang et al. (USPN. 6,235,504) as applied to claims 15-16, 23-26, 31-35, 38-41 above, and further in view of Wittwer et al. (USPN. 6,174,670).

Lowe et al. in view of Zhang et al. teach a method for determining the efficiency of an amplification of a target nucleic acid as discussed above in section 4A.

However, Lowe et al. in view of Zhang et al. did not teach detecting amplified nucleic acid using a DNA- binding dye, SYBR Green I.

Wittwer et al. teach a method for monitoring and quantitating target nucleic acid during PCR, wherein Wittwer et al. disclose that the method utilizes DNA-binding dye, SYBR Green I for monitoring and quantitating target nucleic acid (see col. 7, line 14-31).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of determining the efficiency of amplification and quantitating a target nucleic acid as taught by Lowe et al. in view of Zhang et al. with the step of detecting amplified nucleic acid using SYBR Green I dye as taught by Wittwer et al. to achieve expected advantage of developing an improved sensitive method for quantitating a target nucleic acid because Wittwer et al. taught that SYBR Green I is a preferred double-strand-specific dye for fluorescence monitoring of PCR, primarily because of superior sensitivity, arising from greater discrimination between double stranded and single stranded nucleic acid, and is inexpensive dye (see column 23, line 9-16). An ordinary practitioner would

have been motivated to combine the method of determining the efficiency of an amplification of a target nucleic acid and quantitation of said nucleic acid as taught by Lowe et al. in view of Zhang et al. with the inclusion of the step of detecting amplified nucleic acid using SYBR Green I dye as taught by Wittwer et al. for the purpose of enhancing the sensitivity of the method for quantitation of a target nucleic acid and for cost-effective purposes.

Response to Arguments

5. Applicant's response to the office action is fully considered and is found persuasive.

6. With regard to the rejection made in the previous office action under 35 USC 112, second paragraph, Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein in view of the amendment.

7. With regard to the rejection made in the previous office action under 35 USC 103(a), Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein in view of the persuasive arguments particularly directed to the prior art Meijerink et al. and new grounds of rejections.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Gary Benzion reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
January 25, 2005

JEFFREY FREDMAN
PRIMARY EXAMINER
1/29/05